

Applicants: Mark McCormick, *et al.*  
Application No.: 10/675,329  
Response Dated: October 14, 2008  
Reply to Office Action Dated: April 14, 2008

#### REMARKS

In a final Office Action dated April 14, 2008, the Examiner withdrew rejections of Claims 8, 11 and 12 under 35 U.S.C. §112, second paragraph, withdrew rejections of Claims 7, 8, and 11-13 under 35 U.S.C. §103(b) and withdrew rejections of Claims 7-13 under 35 U.S.C. §103(a). The Examiner also accepted Applicants' new declaration and replacement drawing and properly specified the elected species but asserted that provisional application 60/415,119 filed September 30, 2002 lacks enabling support for an alignment mark formed by a maskless array synthesis instrument. The Examiner imposed new rejections under 35 U.S.C. §112, first and second paragraphs as well as under 35 U.S.C. §§102(b) and 103(a).

Applicants thank the Examiner and Supervisory Examiner Schultz for their time during a personal interview at the US Patent and Trademark Office on October 2, 2008 during which the rejections were discussed as summarized in an Interview Summary dated October 2, 2008.

Applicants each ground of rejection below and respectfully request reconsideration of the merits of the application. A request for continued examination accompanies this response.

#### Priority date

The Examiner refused to accord the application the benefit of the priority date of the provisional application in view of the prior claim language ("alignment mark is formed by a MAS instrument"), but that phrases is removed from the claims. Instead, Applicants here amend step c) of the independent claims to recite that *a protected hapten* is deposited on portions of a microarray using the same maskless array synthesis instrument that is used to deposit the probe sets in step b) of the independent claims, and further that the deposited hapten is deprotected and that a illuminating compound is attached to the deprotected hapten. Applicants also amend dependent claim 10 to properly focus the claim on the reporter molecule.

The Examiner's attention is directed to paragraph [00010] of the provisional patent application which describes an embodiment in which "the illuminating compound is constructed in situ by depositing a compound, such as biotin coupled to a photo-active or chemi-active protecting molecule, in the border region and then coupling the deposited compound to a

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secondary compound, such as streptavidin and a reporter molecule, to render the border visible."

The same paragraph goes on to describe a preferred embodiment in which "the streptavidin is bound to biotin after cleaving from the biotin a protecting molecule, such as phosphoramidite [*sic*], by exposing the combination to a light source, activity or compound that removes the protecting molecule." Paragraph [00018] also describes phosphoramidite being removed to permit binding of the streptavidin molecule.

Accordingly, the provisional application provides the requisite support for the claim as amended, contemplating both chemi- and photoactive deprotection of the deposited hapten (which can be biotin) as well as binding of the illuminating compound to the deposited hapten. As already noted, the utility specification also indicates that the array is removed from the instrument and deprotected. As further noted by the Examiner, Fig. 1 of the utility application depicts a biotin-phosphoramidite bearing DMT, a protecting group that can be removed by chemi-active deprotection once the molecule has been attached to the interstitial region by light-directed deprotection of the array substrate followed by deposition of the molecule via its phosphoramidite portion.

Reconsideration of the refusal to accord the priority date is respectfully requested.

Rejections under §112, first paragraph

The Examiner imposed new matter rejections arising out of Applicants' prior recitation that the alignment mark is formed by the maskless array synthesis instrument. Reconsideration is respectfully requested as the recitation no longer appears in the amended claims, and Applicants have articulated support in the Specification for the amended claim language.

Rejections under §112, second paragraph

The Examiner imposed rejections arising out of Applicants' prior recitation of a "MAS<sup>TM</sup> instrument." Reconsideration is respectfully requested because any uncertainty or lack of clarity in the claims is avoided by Applicants amendments that replace the term with the term "maskless array synthesis."

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#### Rejections under §102

The Examiner rejected Claims 7-11 and 13 as allegedly anticipated by Singh-Gasson (1999). Singh-Gasson cannot anticipate the claims as clarified because it does not teach, as in steps c), depositing a protected hapten on the interstitial region of the microarray, wherein the hapten is deposited by the same maskless array synthesis instrument used to build the probe sets of step b). Instead, Singh-Gasson teaches an otherwise conventional oligonucleotide array to which a haptenylated oligonucleotide target (in Singh-Gasson, a biotinylated *CPK6*-complementary oligonucleotide) is bound in a conventional microarray hybridization. The microarray is subsequently stained with a detection moiety (in Singh-Gasson, streptavidin phycoerythrin) to reveal or visualize hapten on the hybridized target. While these could arguably be considered alignment marks, they are not provided in accord with the claimed method, wherein the hapten is deposited on the microarray in a deprotection/deposition step, like any other, but not via an attached oligonucleotide target. Further, the Examiner's prior reliance upon the separate attachment of a fluorescein border around the array using a fluorescein phosphoramidite is not relevant to the pending claims which more clearly now recite that the detection moiety is attached to the hapten to form the alignment mark(s). Accordingly, Singh-Gasson does not disclose every element of the claimed method and cannot anticipate the claims. Reconsideration is respectfully requested.

#### Rejections under §103

The Examiner rejected Claims 7-13 as allegedly obvious over Singh-Gasson (1999), applied as above, in view of Giegrich et al (1998). Giegrich is said to disclose NPPOC, which is said to be an obvious substitution for the McNPOC of Singh-Gasson. Applicants' comments above about the shortcomings of Singh-Gasson vis-à-vis its inability to anticipate the claimed invention apply with equal force to the rejections imposed under §103. Briefly, Singh-Gasson does not teach the claimed method for forming an alignment mark by depositing a hapten using a maskless array synthesis and then attaching a detection moiety to the deposited hapten. Giegrich is silent as to this aspect of the claimed invention, and accordingly cannot bridge the gap already

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demonstrated to exist between Singh-Gasson and the claimed invention, without regard to Giegrich's teaching about using one phosphoramidite or another in maskless array synthesis. Reconsideration is respectfully requested.

Fees

A Petition for an extension of time for three months accompanies this response so the response will be deemed to have been timely filed. If any other extension is due in this or any subsequent response, please consider this to be a petition for the appropriate extension and a request to charge the petition fee due to Deposit Account No. 17-0055. No other fee is believed due, but if any other fee is due in this or any subsequent response, please consider this to be a request to charge the fee to the same Deposit Account.

Respectfully submitted,

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